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1: Br J Pharmacol. 1989 Sep;98(1):318-24.

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Comparison of the effects of isobutylmethylxanthine and milrinone on ischaemia-induced arrhythmias and platelet aggregation in anaesthetized rabbits.

Holbrook M, Coker SJ.

Department of Pharmacology and Therapeutics, University of Liverpool.

1. The aim of this study was to compare the effects of the non-selective phosphodiesterase (PDE) inhibitor, isobutylmethylxanthine (IBMX) and the selective PDE III inhibitor, milrinone, in a rabbit model of acute myocardial ischaemia. 2. Coronary artery occlusion caused changes in the ST-segment of the ECG and ectopic activity in all control rabbits. Ventricular fibrillation occurred in 10 out of 14 (71%) of these animals. Pretreatment with IBMX 100 micrograms kg⁻¹ plus 10 micrograms kg⁻¹ min⁻¹, starting 10 min before coronary artery occlusion, reduced ischaemia-induced ST-segment changes and ventricular fibrillation occurred in only 10% of this group (n = 10). A similar dose of milrinone had no antiarrhythmic activity, whereas with a lower dose of milrinone, 30 micrograms kg⁻¹ plus 3 micrograms kg⁻¹ min⁻¹ (n = 10), only 30% of rabbits fibrillated and ST-segment changes were attenuated. 3. Acute administration of both IBMX and milrinone reduced arterial blood pressure. With the higher dose of milrinone a significant effect was still present after 10 min of drug infusion. A greater hypotensive response to the higher dose of milrinone was observed in the rabbits which subsequently fibrillated during ischaemia. A marked tachycardia was also observed after administration of the higher dose of milrinone. 4. At the end of the experiment platelet aggregation was studied ex vivo. ADP-induced aggregation was reduced by pretreatment of the rabbits with milrinone but not IBMX. Both PDE inhibitors enhanced the ability of isoprenaline to inhibit ADP-induced platelet aggregation but

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milrinone was more effective, particularly at the higher dose.
(ABSTRACT TRUNCATED AT 250 WORDS)

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